Health-economic evaluation of fluocinolone acetonide 190mg implant in people with diabetic macular edema

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ABSTRACT

Objectives: To assess healthcare resource use and costs of treating people with clinically significant diabetic macular edema (DME) with fluocinolone acetonide (FAc) 190 mg intravitreal implant in routine clinical practice.

Methods: The retrospective Iluvien Clinical Evidence (ICE-UK) study collected data on people prescribed the FAc implant in any one of 13 ophthalmology centers between April 1, 2013 and April 15, 2015. Data were collected for 12 months before and after implantation. Standard UK costs were attributed to healthcare resource use.

Results: In total, 208 people contributing 233 FAc-treated eyes were selected. Mean age was 68.1 years and 62% were male. The mean (standard deviation, SD) number of anti-vascular endothelial growth factor (anti-VEGF) injections per FAc treated eye in the 12 months prior to implant was 2.8 (2.5), decreasing to 0.6 (1.4) for the same period after implant (p< .001). The corresponding figures for other steroid injections (dexamethasone and triamcinolone) were 0.14 (0.4) before and 0.08 (0.4) after implant (p¼ .016). There was no statistically significant difference in the number of laser therapies required in the 12 months before and after FAc implant (mean ¼ 0.12 vs 0.11, respectively; p¼ .626). Overall, mean (SD) healthcare costs were £2,691 (£1,850) before and £1,239 (£1,203) after FAc implant (p< .001). The unit drug and administration cost per FAc implant was £5,680.

Conclusions: Excluding the cost of the FAc implant, healthcare costs were significantly reduced in the 12 months post-implant. FAc implant has a duration of 3 years. This needs to be considered when interpreting the cost associated with the FAc implant.

Introduction

The prevalence of type 2 diabetes is increasing worldwide, due to increasing obesity allied to sedentary lifestyle and a general aging of populations. Diabetic retinopathy, including diabetic macular edema (DME), is the most frequent cause of visual loss and blindness in the working-aged segment of the populations of the developed nations. Increases in this primary cause of visual deterioration will, in turn, lead to a substantial rise in the burden of DME to people with diabetes and healthcare providers alike. It has been estimated that the healthcare cost of managing people with DME in England, UK, alone was £92 million in 2010. However, since the introduction of anti-VEGF and intravitreal steroid injections, this is likely to have increased. Management of DME varies according to the degree of macular thickening, with treatment options including laser photocoagulation, antiVEGF (vascular endothelial growth factor) therapies and intravitreal steroids.

Fluocinolone acetonide (FAc) 190 mg intravitreal implant is a licensed intravitreal steroid injection approved in the UK for the treatment of visual impairment associated with chronic DME in eyes that have been insufficiently responsive to available therapies. A single FAc 190 mg intravitreal implant provides a sustained release of FAc for up to 3 years, and has been shown to be effective over this period. Therefore, compared with intravitreal anti-VEGF therapies, where the doses can be administered as frequently as every 4 weeks, the FAc implant may have a significant impact on resource utilization in busy hospital eye units. Side-effects of FAc included steroid-induced cataracts and raised intraocular pressure (IOP).

Like all other healthcare interventions, treatments for DME need to demonstrate cost-effectiveness. The UK National Institute for Health and Care Excellence (NICE) has confirmed the cost-effectiveness of the FAc implant in eyes with a pseudophakic lens, based on data from FAME. A US economic evaluation using the same data from FAME arrived at an incremental cost-effectiveness ratio (ICER) of $38,763 per quality adjusted life year (QALY) gained, based on the assumption that 40% of people would be treated unilaterally. When it was assumed that 100% of people were treated unilaterally, the FAc implant was found to be cost saving (ICER ¼ –$10,620 per QALY).

The objective of this study was to evaluate healthcare resource use and associated financial costs involved in treating DME in routine clinical practice, both before and after FAc intravitreal implant, using data from the Iluvien Clinical Evidence study in the UK (ICE-UK). The ICE-UK study was conducted in order to assess the effectiveness of FAc intravitreal implant in clinical practice, where people are likely to have been exposed to first line anti-VEGF prior to initiation of steroid therapy, a reflection of current clinical practice. Since the NICE recommendations, which were based on the combined FAME studies, the treatment paradigm for DME has

changed, necessitating further research to be conducted in people prescribed anti-VEGF as first line therapy. Importantly, the ICE-UK study collected data not only after implant, but also in the 12 months prior to implant, bearing in mind that DME typically involves a gradual deterioration in vision. The availability of such data, which are rarely reported, enabled the estimation of healthcare resource use in the 12month periods before and after FAc implant.

Methods

Data source

For this retrospective cohort study, data collected for the ICEUK study were utilized. In brief, data from patient medical records from 13 participating UK ophthalmology departments were extracted, pseudonymized, and combined into a single dataset. Collected data included patient demographics, medical history, implant data, and data from multi-disciplinary and medication reviews in the 12 months before and after implant. Quantitative data were also generated from medical records and administrative records, together with clinical measurements.

Table 1. Unit cost of healthcare resources utilized.

Resource	Cost	Details
Bevacizumab (unlicensed indication)	£48	Cost of Avastin 5 mg/0.2 ml manufactured as an unlicensed special formulation. Personal communication via email from Shakeel Herwitker (shakeel.herwitker@rlbuht.nhs.uk), Royal Liverpool and Broadgreen University Hospital, 17 January 2016.
Aflibercept	£816	dm + d list price for Eylea.
Ranibizumab	£551	dm + d list price for Lucentis.
Dexamethasone	£870	dm + d list price for Ozudex.
Triamcinolone (unlicensed indication)	£1.49	dm + d list price for Kenalog.
Fluocinolone acetonide	£5,500	dm + d list price for Iluvien.
Outpatient appointment	£59	NHS National Tariff 2014–15 WF01A follow-up outpatient attendance follow-up single professional, treatment function 130.
Outpatient procedure for drug administration	£137	National Tariff 2014–15, HRG BZ23Z Vitreous retinal procedure category 1.
Outpatient laser photocoagulation	£137	National Tariff 2014–15, HRG BZ23Z Vitreous retinal procedure category 1.
Outpatient OCT	£137	National Tariff 2014–15, HRG BZ23Z Vitreous retinal procedure category 1.
Glaucoma surgery	£720	NHS National Tariff 2014–15 combined day case/ordinary elective spell tariff. Weighted mean calculated based on number of admissions for each HRG in HES 2014/15. Weighted mean = 26%*1,213 (BZ17Z) + 31%*783 (BZ18Z) + 44%*367 (BZ19Z)
Vitrectomy	£1,097	National Tariff 2014-15, HRG BZ22Z Vitreous retinal procedure category 2.
Cataract operation	£699	HRG BZ02Z Phacoemulsification cataract extraction and lens implant combined day case/ ordinary elective spell tariff. More than one relevant HRG was available. However, as HRG BZ02Z is applied to 95% of cataract operations according to HES 2014–15 data, this was deemed to be the most appropriate HRG for this study.

dm þ d, Dictionary of medicines and devices; NHS, National Health Service; HRG, Healthcare Resource Group; OCT, optical coherence tomography; HES, Hospital Episode Statistics.

Ethical approval

The lead clinician and Caldicott Guardian at each center gave written approval for extraction of anonymized data. The study protocol was approved by the head of research governance at the lead clinical center. This study was conducted in accordance with the Declaration of Helsinki and the UK Data Protection Act.

Subjects

People with type 1 and type 2 diabetes suffering from DME were treated with FAc intravitreal implant in at least one eye as part of their routine care. In order to ensure that subjects were eligible for a minimum follow-up of 12 months postFAc implant, only those implants inserted between April 1, 2013 and April 15, 2015 were included in the study. Other reasons for insufficient follow-up included: non-attendance at the clinic, last appointment missed post-index, patient had left the clinic. Those with insufficient follow-

up or with a history of participating in any interventional study for DME were excluded. Only those people with a 12-month history prior to implant were eligible for inclusion.

Study eyes were defined as eyes treated with FAc implant and comprised first eyes treated with FAc implant (all included people) and, where applicable, second eyes treated with FAc implant, with the index date defined as the date of first recorded FAc intravitreal implant into the study eye. Fellow eyes were defined as eyes that were not treated with FAc implant. Data were collected for the study eyes from 12 months prior to and at least 12 months post-index date.

Outcomes

Healthcare resource use and the corresponding financial costs were estimated for each study eye for the 12-month period both prior to and post-index date. Healthcare resources used on the day of FAc implant were regarded as occurring post-implant. Unit costs applied to healthcare resources are listed in Table 1. The cost of outpatient attendances and procedures and inpatient or day case admissions were derived using the costs detailed in the NHS National Tariff for England, UK. Reviews recorded in the dataset were assumed to have occurred during an outpatient attendance. Outpatient procedures recorded in the dataset comprised: administration of treatments for DME (anti-VEGF, steroids, and macular laser therapy) and ocular coherence tomography (OCT).

Drug costs for treatments for DME were taken from the current price listed in the NHS Dictionary of Medicines and Devices (dm þ d) database. Costs for bevacizumab were not listed in the dm þ d database, because no licensed formulation of bevacizumab is available in the UK for treatment of DME. Instead, unit costs for this drug were obtained from the Royal Liverpool and Broadgreen University Hospital, manufacturers and suppliers of an unlicensed formulation of bevacizumab.

The costs of inpatient or day case admissions for cataract operations, glaucoma surgery, or vitrectomies were taken from the NHS National Tariff for England, UK. Where more than one procedure was carried out on the same date, the NHS HRG4 (Healthcare Resource Group 4) 2014/15 payment grouper was used to determine the most appropriate HRG. Procedures and reviews listed on the same date as an inpatient admission were assumed to have been carried out as part of the inpatient admission. Similarly, where an inpatient or day case procedure was listed for the fellow eye, procedures carried out in the study eye were assumed to have taken place as part of the inpatient or day case admission. Procedures carried out in first eyes treated with the FAc implant were taken into account when determining the cost of procedures carried out in the second treated eye. For example, if a DME treatment was administered to both the first FAc treated eye and second FAc treated eye on the same date, the cost applied to the first eye included both the cost of administering the drug as part of an outpatient attendance and the drug cost, whereas the cost applied to the second eye comprised the drug cost only.

The class of IOP-lowering therapy prescribed to an individual was documented at the time of review, but no prescription information (e.g. product, dose, quantity or date prescribed) was recorded. The maximum dose of each IOP medication for each recorded class was taken from the British National Formulary and the volume of eye drops required per 28 days, which covers the shelf life of IOP-lowering drops, was calculated based on previously published data or an estimate of 20 drops per milliliter. The need for bilateral treatment with the same drug classes was taken into account in the calculation. A cost per day was generated for each IOP-lowering product listed in the Prescription Cost Analysis (PCA) for England 2015. A weighted average cost per class per day was then generated based on the number of items of each product dispensed in the PCA 2015. Where an eye was treated with more than one IOP-lowering class at any one time, it was assumed that combination products would have been prescribed where available.

Statistical analysis

Costs were compared before and after index date using the Wilcoxon signed ranks test because healthcare resource use and costs were not normally distributed. Statistical analyses were carried out using IBM SPSS Statistics version 20. The costs are detailed as their mean value and standard deviation (SD), as per convention.

Table 2. Characteristics at FAc implant.

Parameter	Value
Subjects, n	208
First eyes treated, n (%)[a]	208 (89%)
Second eyes treated, n (%)[b]	25 (11%)
All treated eyes, n (%)	233
Patient characteristics	
Age last clinic visit, mean (SD)[c]	68.1 (10.7)
Males, n (%)	128 (62%)
Type 2 diabetes, n (%)	176 (85%)

Oral anti-hyperglycemic agents	76 (43%)
Insulin	43 (24%)
Insulin plus oral anti-hyperglycemic agents	57 (32%)
Type 1 diabetes, n (%)	32 (15%)
Oral anti-hyperglycemic agents	0 (0%)
Insulin	28 (88%)
Insulin plus oral anti-hyperglycemic agents	4 (13%)
Number of years with diabetes, median (IQR)[c]	18 (11–27)
Eye characteristics	
Pseudokaphic lens status, n (%)[d]	205 (88%)
Visual acuity	
n (%)	224 (96%)
Median (IQR), LogMAR units	0.66 (0.48–1)
Visual acuity	
n (%)	224 (96%)
Median (IQR), ETDRS letters	52 (35–61)
Centre subfield thickness	
n (%)	198 (85%)
Median (IQR), lm	447 (352–587)
Central foveal thickness	
n (%)	191 (82%)
mean (SD), lm	482 (186)
IOP n	
(%)	185 (79%)
Median (IQR), mmHg	15 (13–18)
Prior macular laser	
treatments n (%)	146 (63%)
Median (IQR)	1 (0–1)
Prior anti-VEGF injections	
n (%)	191 (82%)
Median (IQR)	3 (1–6)
Prior ranibuzimab injections	
n (%)	162 (70%)
Median (IQR)	3 (0–5)
Prior aflibercept injections	
n (%)	1 (0%)
Median (IQR)	0 (0–0)
Prior bevacizumab injections	
n (%)	74 (32%)
Median (IQR)	0 (0–1)
Prior steroid injections	
n (%)	101 (43%)
Median (IQR)	0 (0–1)
Prior dexamethasone	
injections n (%)	17 (7%)
Median (IQR)	0 (0–0)
Prior triamcinolone	
injections n (%)	88 (38%)
Median (IQR)	0 (0–1)
IOP-lowering medication, n (%)	42 (18%)
Prostaglandin analogs, n (%)	26 (11%)
Beta blockers, n (%)	17 (7%)
Alpha agonists, n (%)	5 (2%)
Carbonic anhydrase inhibitors, n (%)	5 (2%)
Other, n (%)	8 (3%)

SD, standard deviation; IQR, interquartile range; LogMAR, Logarithm of the Minimum Angle of Resolution; VEGF, vascular endothelial growth factor; IOP, intraocular pressure.

Results

Patient characteristics at FAc implant

Two hundred and eight people were eligible for inclusion in the study, contributing 233 FAc treated eyes; 208 (89%) eyes were first eyes treated with FAc implant. Mean (SD) age at implant was 68.1 (10.7) years and 62% of people were male; 15% of people had type 1 diabetes and 85% of people had type 2 diabetes (Table 2).

In total, 205 (88%) treated eyes had a pseudophakic lens prior to FAc implant (Table 2). Median (interquartile range, IQR) visual acuity was 0.66 (0.48–1.00) LogMAR units at the time of implant. Mean (SD) central foveal thickness was 428 (186) mm. One hundred and forty-six (63%), 191 (82%), and 101 (43%) subjects had previously been treated with macular laser therapy, anti-VEGF therapy, or steroids other than FAc prior to the insertion of the FAc implant.

Healthcare resource use and costs in the 12 months prior to and post-FAc implant

Healthcare resource use and costs in the 12 months prior to and post-FAc intravitreal implant are detailed in Table 3. FAc treated eyes were prescribed significantly ($p < .001$) more anti-VEGF therapies in the 12 months prior to FAc implant compared with the 12-month period post-implant (mean [SD] ¼ 2.8 [2.5] vs 0.6 [1.4] injections). The number of steroid injections per eye was also higher in the 12 months prior to implant (mean [SD] ¼ 0.14 [0.4] vs 0.08 [0.4], p ¼ .016). However, there was no statistically significant difference in the number of laser therapies required per eye in the 12 months prior to and post-FAc implant (mean ¼ 0.12 vs 0.11, respectively, p ¼ .626). When compared with the 12-month period post-FAc implant, the number of vitrectomies (mean ¼

0.06 vs 0.02, p ¼ .022), cataract operations (mean ¼ 0.24 vs
0.07, $p < .001$), and outpatient appointments (mean ¼ 6.7 vs 6.2, $p < .033$) were all higher in the 12-month period prior to implant. There was no statistically significant difference in the number of OCT scans carried out in the 12 months before and after FAc implant (mean [SD] ¼ 3.6 [2.7] vs 3.5 [2.2], p ¼ .987).

When the drug and administration costs associated with prescribing the FAc implant were included in the cost estimate, the overall healthcare cost was higher in the 12 months following FAc implant (mean ¼ £6,919 vs £2,691, $p < .001$; Table 3). However, excluding the drug and administration costs associated with prescribing the FAc implant, overall healthcare costs were higher in the 12 months period prior to FAc implant (£1,239 vs £2,691, $p < .001$).

The mean number of concomitant treatments for DME prescribed per eye was higher for each of the four quarters prior to implant when compared with the four quarters after implant (Figure 1(a)). The mean number of cataract surgeries carried out per eye was highest in each quarter prior to FAc implant and in the first quarter post-implant (Figure 1(b)). However, it is important to note that 15 out of 17 surgeries recorded in the first quarter post-FAc implant were carried out on the same day as the implant was inserted. The mean number of vitrectomies carried out per eye for each quarter remained low for the 12 months prior to and post-FAc implant, and only two glaucoma surgeries were recorded in the 12 months following implant. As anticipated, the mean number of outpatient attendances per eye was highest in the first quarter post-FAc implant (including the outpatient appointment attended to administer the implant, Figure 1(c)). The lowest mean number of outpatient attendances was observed in quarters 2, 3, and 4 post-implant. Excluding the drug and administration costs associated with prescribing the FAc implant, observed healthcare costs were lower in each of the four quarters post-implant when compared with the same period prior to implant (Figure 1(d)). This was largely due to a decrease in the mean number of additional anti-VEGF and steroid therapies prescribed, which resulted in a corresponding decrease in DME treatment and administration costs. The mean drug and administration cost associated with prescribing the FAc implant was £5,680.

Table 3. Healthcare resource use and costs before and after FAc implant.

	Prior to implant		Post-implant[a]		p-value
	n	Mean (SD)	n	Mean (SD)	
Healthcare resource use					
Ranibizumab	607	2.6 (2.5)	122	0.5 (1.4)	<.001
Bevacizumab	37	0.2 (0.7)	2	0.0 (0.1)	<.001
Aflibercept	5	0.0 (0.3)	17	0.1 (0.6)	.244
Dexamethasone	6	0.0 (0.2)	4	0.0 (0.2)	.317
Triamcinolone	27	0.1 (0.3)	15	0.1 (0.3)	.028
Laser photocoagulation	28	0.1 (0.4)	25	0.1 (0.4)	.626
FAc implant	0	0.0 (0)	233	1.0 (0)	<.001
OCT	828	3.6 (2.7)	812	3.5 (2.2)	.987
Glaucoma surgery	0	0.0 (0)	2	0.0 (0.1)	.157
Vitrectomy	15	0.1 (0.3)	4	0.0 (0.1)	.022
Cataract surgery	56	0.2 (0.4)	17	0.1 (0.3)	<.001
Outpatient appointments	1,556	6.7 (3.1)	1,454	6.2 (2.8)	.033
Healthcare costs, £					
Overall	627,058	2,691 (1,850)	1,612,184	6,919 (1,195)	<.001
Overall excluding FAc implant	627,058	2,691 (1,850)	288,702	1,239 (1,203)	<.001

SD, standard deviation; FAc, fluocinolone acetonide; OCT, ocular coherence tomography.

[a]Healthcare resources used on the day of FAc implant and their corresponding costs are included in the post-implant healthcare resource use and cost estimates.

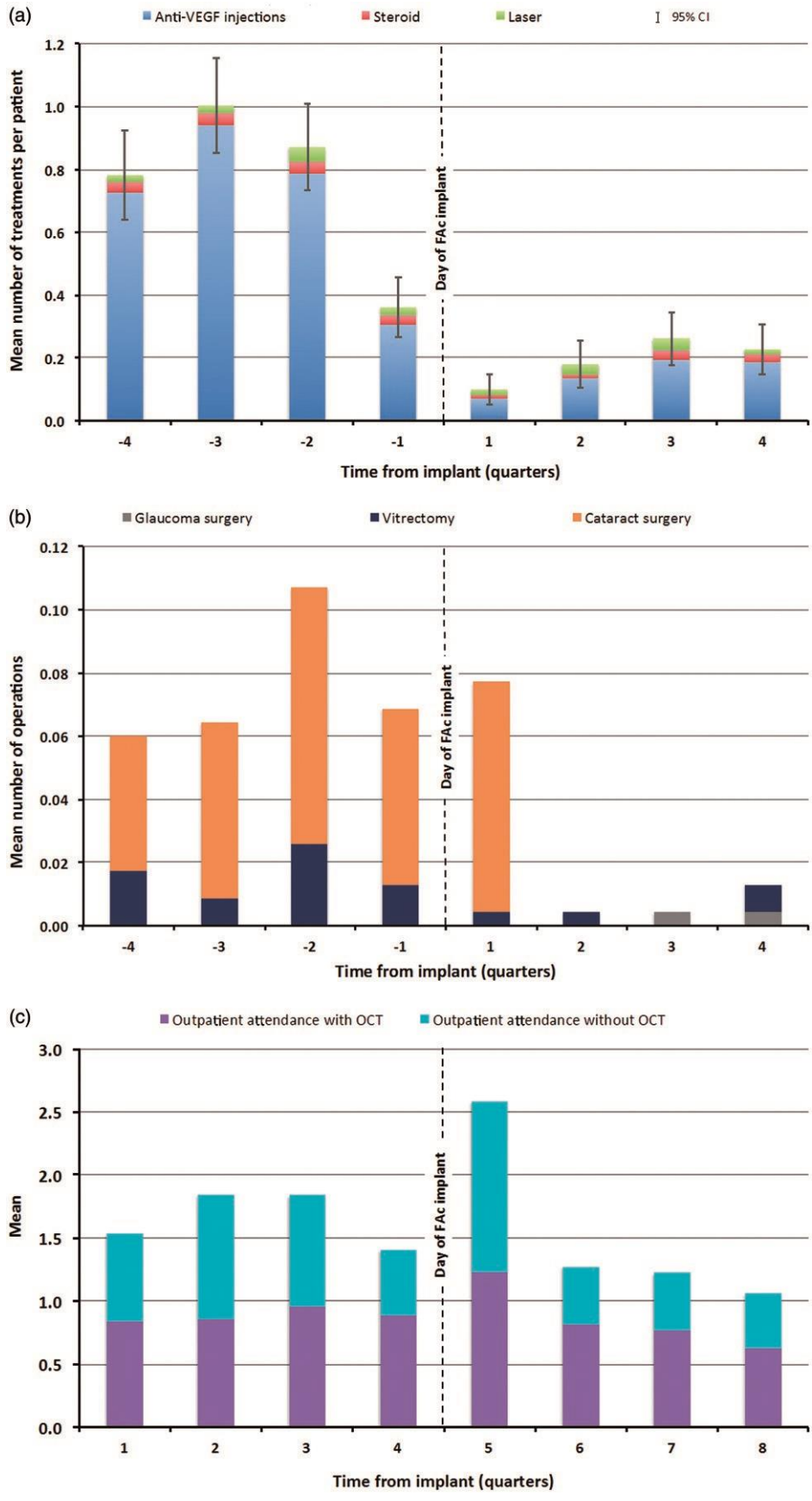
(a)
Anti-VEGF injections
Steroid
Laser
95% CI
Mean number of treatments per patient
1.2
1.0
0.8
0.6
0.4
0.2
0.0
Day of FAc implant
-4
-3
-2
-1
1
2
3
4
Time from implant (quarters)
(b)
Glaucoma surgery
Vitrectomy
Cataract surgery
Mean number of operations
0.12
0.10
0.08
0.06
0.04
0.02
0.00
Day of FAc implant
-4
-3
-2
-1
1
2
3
4
Time from implant (quarters)
(c)
Outpatient attendance with OCT
Outpatient attendance without OCT
Mean
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Day of FAc implant
1
2
3
4
5
6
7
8
Time from implant (quarters)

Figure 1. Quarterly updated healthcare resource use and costs in the 12 months prior to and post-FAc implant. (a) Mean number of treatments per eye for diabetic macular edema; (b) Mean number of daycase and inpatient admissions per eye; (c) Mean number of outpatient attendances per eye (including outpatient attendances for FAc implant); (d) Mean healthcare cost per eye, per quarter. VEGF, vascular endothelial growth factor; OCT, ocular coherence tomography; IOP, intraocular pressure. Healthcare resources used on the day of FAc implant and their corresponding costs are included in the post-implant healthcare resource use and cost estimates.

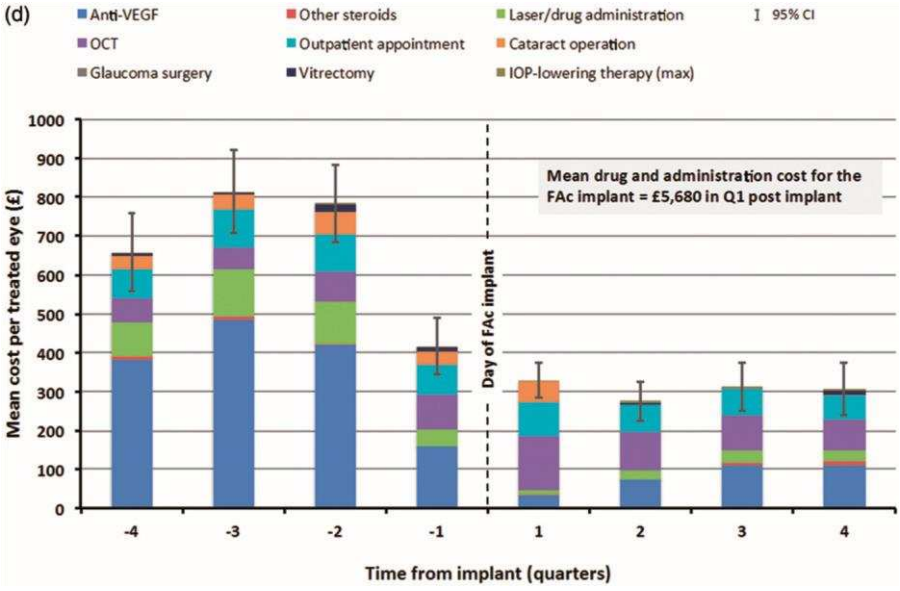

Figure 1. Continued.

Discussion

Statistically significant reductions in anti-VEGF therapies, steroid therapies, outpatient appointments, and vitrectomies were observed in the 12 months following FAc implant when compared with the 12 months prior to implant. Excluding the cost of the actual FAc intravitreal implant and the cost associated with its insertion, healthcare resource costs were halved (from £2,691 to £1,239) in the 12 months following the FAc implant compared with the 12 months before implant. However, when the cost of FAc implant was included, post-implant cost was higher than the cost prior to implant. The drug and administration cost associated with inserting the FAc implant was £5,680, but, due to its prolonged duration of action, no drug and administration costs for the FAc implant should be incurred in the subsequent 3 years, only those costs associated with monitoring and managing adverse events. Using data from the ICE-UK study, we have previously reported that 45%, 32%, and 21% of FAc treated eyes improved by 5, 10, and 15 ETDRS letters at 12 months post-FAc implant, respectively, despite a mean decrease in visual acuity and central foveal thickness in the year prior to FAc implant. In addition to the visual benefits observed over the first 12 months following implant, sustained improvements in visual acuity were observed for up to 3 years post-implant.

When the cost of the FAc intravitreal implant was excluded, the reduction in cost observed post-implant was largely due to a reduction in the frequency of anti-VEGF therapy and its administration. No significant change in the number of laser treatments administered prior to and postimplant was observed and three of the study sites did not allow for anti-VEGF use after FAc implantation. The Diabetic Retinopathy Clinical Research Network reported a steady decrease in the number of ranibizumab injections administered over the trial's 5-year follow-up period, with no corresponding decrease in visual acuity. In the FAME study, the use of laser and anti-VEGF treatments was more common in the sham (untreated) arm of the study compared with FAc 0.2 mg/day. Conversely, as FAc 190 mg intravitreal implant is only licensed in eyes that have been insufficiently responsive to other therapies, the reduction in the use of anti-VEGF therapies in the 12 months post-implant may reflect prior non-response to these agents. Previous insufficient responsiveness to available DME therapies was not a requirement for selection into the FAME study; however, a decrease in anti-VEGF therapy was still observed. Intensive intravitreal injection regimens have been previously reported to have an effect on the quality of life of people with DME.

Compared with anti-VEGF therapies, the FAc implant has the advantage of requiring substantially less frequent intravitreal injections, and, therefore, improved patient compliance, reduced treatment burden, and reduced resource use have been previously cited as possible advantages. However, monitoring for complications is recommended 2–7 days after insertion of the implant, and then at least quarterly thereafter, necessitating regular visits to the ophthalmology outpatient department. However, in this study, a small but significant decrease in the number of outpatient appointments was observed, perhaps owing to the reduction in the number of anti-VEGF intravitreal injections administered. No significant difference in the number of OCT scans carried out was observed prior to and post-implant.

Side-effects associated with steroids as a class include cataracts and raised IOP. However, the cost of IOP-lowering medication, monitoring, and glaucoma surgery both before and after implant represented a very small segment of the overall cost of DME care. More cataract operations were recorded prior to FAc implant, and most treated eyes had a pseudophakic lens at the time of implant. This is most likely to be due to the NICE recommendation in the UK that the FAc intravitreal implant be used only in eyes with a pseudophakic lens. Yang et al. have shown that similar or possibly better outcomes can be achieved in those undergoing cataract surgery following FAc implantation compared with pseudophakic eyes treated with FAc implant.

Several studies have reported on the cost-effectiveness of treatments for DME. Pershing et al. investigated the costeffectiveness of laser monotherapy or anti-VEGF or triamcinolone alone or in combination with laser therapy in diabetic macular edema, and reported that costs were reduced with all interventions except laser monotherapy; the number of quality-adjusted life years (QALYs) increased for all interventions except for triamcinolone monotherapy. Bevacizumab is cheaper than aflibercept or ranibizumab, but remains unlicensed for DME. However, bevacizumab has been demonstrated to be more cost-effective than aflibercept and ranibizumab in DME. The FAc intravitreal implant was approved by NICE for the management of DME in eyes with an artificial lens and licensed for the treatment of DME that is insufficiently responsive to other available therapies. The NICE Appraisal Committee determined that, in eyes with a pseudophakic lens, the incremental cost-effectiveness ratio (ICER) of FAc was between £17,500–£30,000 per QALY gained, depending on the utilities used and providing that the FAc implant was supplied under the terms of the patient access scheme. NICE concluded that FAc intravitreal implant in pseudophakic eyes was, therefore, a cost-effective use of NHS resources. In an economic evaluation of the FAc implant by Moore et al., based on the results of the FAME studies, the expected incremental cost-effectiveness ratio for treatment with an FAc implant was reported to be $38,763 (£30,800) when 40% of people are treated unilaterally, and cost-saving (ICER ¼ –$10,620 per QALY) when 100% of people are treated unilaterally.

Strengths and limitations

Advantages and disadvantages of the ICE-UK study have been discussed previously. As this is an observational study, several limitations may occur. Misclassification of outcomes, effectiveness, and safety may have occurred, although data were taken from patient notes and electronic medical records. Retrospective studies are subject to confounding, and can only be used to infer association and not causation. Duration of DME at the time of implant was not recorded. It was not possible to determine the individual's exact age or their duration of diabetes at implant, because these were recorded at their last clinic visit only, the date of which was not supplied. Discrepancies between lens status and cataract operations were observed and have been discussed previously. As it was important to determine the date of any intervention or procedure, recorded cataract operations were included in the study, but lens changes were not. This may have led to an under-estimation of the number and total cost of cataract operations. The recording of procedures occurring near to the end of the study observation period (April 15, 2016) may not be complete as it was possible for procedure dates to pre-date review dates. Analysis was restricted to 12 months' follow-up post-implant, because available follow-up after this date varied from person to person. No cost was applied to IOP-lowering medication when the class prescribed was specified as "other".

First and second treated eyes from the same person were analyzed as independent observations. However, second eyes may be more likely to be treated with FAc implant if the subject had a positive response to treatment in the first eye. In addition, treatment of the second eye may be more likely to occur at certain treatment centers.

Certain assumptions were made in costing ranibizumab, which is available as both a pre-filled syringe and a vial. The pre-filled syringe is designed to be used for the treatment of a single eye. The vial is available as a vial plus injection kit, a vial only pack, and a vial plus filter needle pack. It was assumed that, for bilateral treatment with the same drug on the same date, different product packs would be used to treat each eye when the same drug was administered bilaterally on the same date.

Another limitation is that ranibizumab, aflibercept, and FAc intravitreal preparations indicated for DME are listed on the NICE Patient Access Scheme list and supplied to the NHS at a discounted rate. In this study, however, the list price of the drug was used, as any price agreements between the manufacturer and the Department of Health under the Patient Access Scheme are not publicly available.

Conclusion

The ICE-UK study was designed to investigate the real-world effectiveness of FAc 190 mg intravitreal implant. Various standard clinical outcomes of care for DME when treated with the FAc implant are reported in this supplement. Most of the study eyes included in the study had been treated with anti-VEGFs prior to FAc implantation, and mean visual acuity in the 12 months prior to FAc implant declined. Following intravitreal implantation, vision improved on average to a modest extent. Whilst it improved in some people, it at least stabilized with no further deterioration in the majority of the remaining subjects. During the 12-month follow-up period, 30% of patients were prescribed concomitant treatments for DME. In this study we report that, following exclusion of the cost of the FAc implant itself, there was a corresponding decrease in healthcare resource usage over this period compared with the 12 months prior to implant. The cost of treating raised intraocular pressure was relatively low. Bearing in mind that this disease process typically involves increasing visual morbidity over time, and that the FAc implant functions for at least 3 years, it is likely that there will be an overall cost saving over this extended period, as has been reported in a previous economic evaluation. Furthermore, patient benefits include a lesser need for more frequent anti-VEGF treatments, although the FAc implant is recommended for use in eyes that have already shown an insufficient response to these therapies. Following a single administration, the FAc implant improves or maintains visual acuity and, thus, the quality of life of the recipient over an extended period of time. Therefore, the FAc implant provides the next logical step in the treatment algorithm of resistant DME.